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Oxidative Activities of Mouse Melanomas with Reference to Melanization.

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Dopa Oxidase. In the absence of added cytochrome C, Harding-Passey mouse melanoma homogenates oxidized tyrosine, dopa and catechol, with consumption of oxygen gas and formation of dark brown or black coloration. Cloudman S91 melanoma homogenates acted likewise on dopa and catechol. Tyrosine was oxidized either not at all or following a variable lag period. Similarly prepared homogenates of the derived Algire partially amelanotic melanoma S91A did not measurably oxidize any of the phenols or produce browning, nor did they retard the oxidation of dopa by S91 homogenates to which they were added. Normal liver homogenates behaved like the S91A extracts.

Cytochrome Oxidase. In the presence of added cytochrome C, oxidation of dopa was markedly increased in the S91 melanoma homogenates, and also now occurred extensively in the S91A amelanotic melanoma and liver homogenates. This second type of dopa oxidation took place via cytochrome oxidase, not only because cytochrome C was required but because the action could be eliminated entirely by pretreatment of the homogenates with 70% ethyl alcohol, a treatment that did not decrease true dopa oxidase activity, in fact, often enhanced it, suggestive of elimination of a dopa oxidase inhibition. In no instance was tyrosine oxidized by the cytochrome system.

A third type of melanization was observed in S91AB derivatives of S91A tumors that were obtained by prolonged transfer of the latter in brown dba mice instead of white C mice. Such tumors eventually became highly pigmented, but their homogenates at this stage oxidized dopa only in the presence of added cytochrome C. However, homogenates of later transfers gradually came to show, without added cytochrome C, endogenous dopa oxidation enhanced by the alcohol treatment, indicating eventual development of true dopa oxidase activity in addition to oxidation via cytochrome oxidase. None of the amelanotic tumors, or their secondarily melanized derivatives, oxidized tyrosine except the S91AB tumor that had undergone prolonged passage (35 generations) in dba mice. In this instance oxidation was not manometrically detectable within the first 4 hours although the extracts to which tyrosine had been added blackened after ca. 24 hours.

Even though the S91AB tumor, maintained by prolonged transplantation in dba mice, assumed the enzymic pattern of the original metastatic S91 tumor, it remained biologically distinct. Thus like the original S91A amelanotic tumor, from which it was derived, it gave no evidence of producing metastases.

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